

We claim:

1. A method of diagnosing or predicting susceptibility to an autoimmune disease in an individual, comprising determining the presence or absence in said individual of a 2-2-4 haplotype at the Notch 4, HSP70-HOM and D6S273 loci,

wherein the presence of said 2-2-4 haplotype is diagnostic of or predictive of susceptibility to said autoimmune disease.

2. The method of claim 1, wherein said autoimmune disease is an inflammatory bowel disease.

3. The method of claim 2, wherein said inflammatory bowel disease is Crohn's disease.

4. The method of claim 1, wherein said autoimmune disease is selected from the group consisting of rheumatoid arthritis and Type I diabetes mellitus.

5. The method of claim 1, wherein said individual is an Ashkenazi Jew.

6. The method of claim 1, wherein determining the presence or absence of the 2-2-4 haplotype comprises enzymatic amplification of nucleic acid from said individual.

7. The method of claim 6, wherein determining the presence or absence of the 2-2-4 haplotype further comprises electrophoretic analysis.

8. The method of claim 6, wherein determining the presence or absence of the 2-2-4 haplotype further comprises restriction fragment length polymorphism analysis.

5           9. The method of claim 6, wherein determining the presence or absence of the 2-2-4 haplotype further comprises sequence analysis.

10           10. The method of claim 1, wherein determining the presence or absence of the 2-2-4 haplotype comprises:

10           (a) obtaining material comprising nucleic acid including Notch4, HSP70-HOM and D6S273 loci from said individual;

15           (b) enzymatically amplifying said nucleic acid to produce a first amplified fragment comprising said Notch4 locus;

            (c) enzymatically amplifying said nucleic acid to produce a second amplified fragment comprising said HSP70-HOM locus; and

20           (d) enzymatically amplifying said nucleic acid to produce a third amplified fragment comprising said D6S273 locus.

            11. The method of claim 10, wherein determining the presence or absence of the 2-2-4 haplotype further comprises:

25           (e) electrophoresing said first amplified fragment, thereby determining whether a Notch4 allele 2 is present;

(f) electrophoresing said second amplified fragment, thereby determining whether a HSP70-HOM allele 2 is present; and

5 (g) electrophoresing said third amplified fragment, thereby determining whether a D6S273 allele 4 is present,

wherein the presence of said Notch4 allele 2, said HSP70-HOM allele 2 and said D6S273 allele 4 indicates that said 2-2-4 haplotype is present.

10 12. The method of claim 10, wherein step (c) further comprises restricting said second amplified fragment with Nco I or an isoschizomer thereof.

15 13. A method of diagnosing or predicting susceptibility to Crohn's disease in an individual, comprising determining the presence or absence in said individual of a disease-associated haplotype associated with a 2-2-4 haplotype at the Notch 4, HSP70-HOM and D6S273 loci,

20 wherein the presence of said disease-associated haplotype is diagnostic of or predictive of susceptibility to Crohn's disease.

25 14. The method of claim 13, wherein said disease-associated haplotype is associated with said autoimmune disease with an odds ratio of at least 5 and a lower 95% confidence limit greater than 1.

15. The method of claim 13, wherein said individual is an Ashkenazi Jew.

16. The method of claim 13, wherein determining the presence or absence of the 2-2-4 haplotype comprises enzymatic amplification of nucleic acid from said individual.

5 17. A method of diagnosing or predicting susceptibility to Crohn's disease in an individual, comprising determining the presence or absence in said individual of a disease-associated allele associated with a 2-2-4 haplotype at the Notch 4, HSP70-HOM and D6S273 loci,

10 wherein the presence of said disease-associated allele is diagnostic of or predictive of susceptibility to Crohn's disease.

15 18. The method of claim 17, wherein said disease-associated allele is associated with said autoimmune disease with an odds ratio of at least 5 and a lower 95% confidence limit greater than 1.

20 19. The method of claim 17, wherein said individual is an Ashkenazi Jew.

25 20. The method of claim 17, wherein determining the presence or absence of the 2-2-4 haplotype comprises enzymatic amplification of nucleic acid from said individual.